

### **REMARKS**

Claims 55-64 and 71 are currently pending in this application for the Examiner's consideration and review. Applicants appreciate the Examiner vacating the Office Action, mailed September 6, 2002, which inadvertently omitted examination of claim 71, and replacing it with the pending Office Action. Claims 55 and 71 were amended, as suggested by the Examiner, to replace the word "such" with --said--. No new matter has been added.

### **The Invention**

The invention relates to methods of treating apnea or apnea disorders in a patient, which comprise administering to a patient in need of such treatment a therapeutically effective amount of (+) norcisapride, or a pharmaceutically acceptable salt thereof, substantially free of its (-) stereoisomer. The invention further relates to methods of preventing or managing apnea or apnea disorders in a patient, which comprises administering to a patient in need of such prevention or management a therapeutically effective amount of (+) norcisapride, or a pharmaceutically acceptable salt thereof, substantially free of its (-) stereoisomer.

### **The Rejections under 35 U.S.C. §112 Should Be Withdrawn**

On page 2 of the Office Action, claims 55-64 and 71 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to enable one of ordinary skill in the art to treat, manage, or prevent apnea or apnea disorders. Applicants respectfully traverse the rejection.

It is well settled law that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Teletronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). Indeed, "[a] patent need not teach, and preferably omits, what is well known in the art." Manual of Patent Examining Procedure (MPEP) §2164.01 (February, 2000). Furthermore, "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." MPEP §2164.01(b), citing *In re Fisher*, 427 F.2d 833 (CCPA 1970).

Applicants respectfully submit that the application, as filed, does indeed enable one of ordinary skill in the art to treat, manage, and prevent apnea and apnea disorders. Applicants have set forth the population of patients to which the invention pertains; specifically, Applicants have indicated that the methods of the invention for treating, preventing, or managing apnea or apnea disorders can be used in males and females, including children and adults. Applicants have further defined preferred embodiments of the invention, which include but are not limited to, treating, preventing, or managing apnea and apnea disorders in obese men and obese men not cl, suffering from obstructive apnea. See Specification at page 8, lines 19-24.

Applicants have further disclosed dosing regimens (e.g., single or divided doses, one to four times per day), dosage ranges and preferred dosage ranges (e.g., 1 mg to about 100 mg), and routes of administration and preferred routes of administration (e.g., oral dosage forms). See Specification at page 11, lines 7-26. In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

On page 2 of the Office Action, claims 55-64 and 71 were also rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. Particularly, the Examiner alleged that it is not clear how apnea and apnea disorders distinguish over each other. Applicants respectfully traverse the rejection.

The primary purpose of the requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent.

A fundamental principle contained in 35 U.S.C. § 112, second paragraph, is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art. MPEP § 2173.01.

Applicants respectfully submit that the claim terms “apnea and apnea disorders” are clearly defined in the specification, as filed. Particularly, Applicants have indicated “apnea is defined in *Stedman’s Medical Dictionary*, 26<sup>th</sup> Edition, William and Wilkins (1995), as the absence of breathing.” See Specification at page

1, lines 9-10. Moreover, Applicants have specifically set forth and described various examples of apnea disorders including, but not limited to, central apnea, deglutition apnea, obstructive or peripheral apnea, sleep apnea, and sleep induced apneas. *Id.* at page 1, lines 15-33. Therefore, Applicants have indeed clearly pointed out and distinctly set forth what Applicants regard as the invention. Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

### **The Rejection under 35 U.S.C. §103 Should Be Withdrawn**

On pages 3-4 of the Office Action, the Examiner rejected claims 55-64 and 71 as allegedly being obvious over U.S. Patent 5,739,151 to McCullough *et al.* ("McCullough") and Skinner, *Tex. Medic.*, 94(9):57-58 (1998) ("Skinner"). In particular, the Examiner indicated that McCullough discloses that (+) norcisapride is useful to treat gastromotility dysfunction, and Skinner discloses that gastromotility dysfunction causes apnea. The Examiner alleged it would therefore be obvious to one of ordinary skill in the art to treat gastromotility dysfunction with (+) norcisapride in a patient having apnea and such treatment would also treat apnea and prevent episodes of apnea. Applicants respectfully traverse the rejection.

The Federal Circuit has set forth three basic criteria that must be met to establish a case of *prima facie* obviousness. First, there must have been at the time of the invention a motivation to combine or modify the teachings of the references cited. *Ecolochem, Inc., v. Southern California Edison Company*, 227 F.3d 1361, 1372 (Fed. Cir. 2000) (holding obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination); *See also, In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988) (holding that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art). Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. *In re Royka*, 490 F.2d 981 (CCPA 1974) (holding that to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) (holding that the teaching or suggestion to make

the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure). Third, there must have been at the time of the invention a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-1208 (Fed. Cir.), cert. denied 502 U.S. 856 (1991) (holding that obviousness requires references to show that there was, at the time of the invention, a reasonable expectation of success).

The legally required suggestion of each and every element of the pending claims (*i.e.*, a method of treating, preventing, or managing apnea or apnea disorders in a patient by administering a therapeutically effective amount of (+) norcisapride, substantially free of its (-) stereoisomer) is not present in McCullough alone or in combination with Skinner. Specifically, McCullough discloses a method of treating a condition caused by gastrointestinal motility dysfunction in a human, which comprises administering to a human in need of treatment of gastrointestinal motility dysfunction, a therapeutically effective amount of (+) norcisapride, or a pharmaceutically acceptable salt thereof, substantially free of its (-) stereoisomer. McCullough further discloses that conditions caused by gastrointestinal motility dysfunction include, but are not limited to, dyspepsia, gastroparesis, constipation, postoperative ileus, and intestinal pseudo-obstruction. *See* Col. 7, lines 17-27. There is no disclosure or suggestion in McCullough of treating apnea or apnea disorders using norcisapride, much less (+) norcisapride substantially free of its (-) stereoisomer.

Skinner does not remedy the deficiencies of McCullough. Skinner is directed to apnea in neonates. Particularly, Skinner discloses that apnea is common in the neonatal period and is most frequently associated with prematurity. This condition is seen also in term infants, especially those with physiological instability, infection, hypoglycemia, drug exposure, intracranial pathology, and gastroesophageal reflux ("GER"). *See* page 1, ¶ 1. Skinner further discloses that apnea can be associated with GER. The mechanism by which GER causes apnea is thought to be mediated by chemoreceptors around the larynx that respond to the gastric acid by causing a reflux central apnea, bradycardia, and pallor. *Id.* pages 1-2. Skinner does not disclose or suggest treating, preventing, or managing apnea or apnea disorders using norcisapride or either of its stereoisomers. Although Skinner discloses that apnea can be induced by GER, Skinner fails to disclose treating apnea with (+) norcisapride.

The motivation to combine or modify the teachings of the references to obtain the claimed invention is clearly absent. In order to establish such motivation to combine or modify the teachings of references, it is well settled law that "there must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination." *In re Oetiker*, 977 F.2d 1443 (Fed. Cir. 1992). The legally required suggestion of each and every element of the pending claims (*i.e.*, a method of treating, preventing, or managing apnea or an apnea disorder using (+) norcisapride) is not present in McCullough or Skinner alone or in combination. *Ecolochem, Inc., v. Southern California Edison Company*. The mere fact that McCullough discloses treating gastrointestinal motility dysfunction using (+) norcisapride, and Skinner discloses apnea caused by GER in neonates would not provide the legally required motivation to combine the cited references. Moreover, as the Board has asserted in *Ex parte Clapp*, "[t]o support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the Examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." Applicants submit that there is neither an express or implicit suggestion of the claimed invention in the references, nor does the Examiner present any convincing reasoning why the claimed invention is obvious. Instead, the Examiner relies on hindsight in reaching his obviousness determination. The Federal Circuit has stated that when prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than hindsight obtained from the invention itself. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132 (Fed. Cir. 1985). (holding that it is error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a blueprint).

Even with the aid of impermissible hindsight the claimed methods of treating, preventing, or managing apnea or apnea disorders cannot be identified from McCullough alone or in combination with Skinner. McCullough merely discloses a method of treating a condition caused by gastrointestinal motility dysfunction using a therapeutically effective amount of (+) norcisapride, substantially free of its (-) stereoisomer. McCullough does not disclose or suggest a method of treating, preventing, or managing apnea or apnea disorders using (+) norcisapride, nor would a

combination of the references provide such disclosure or suggestion. Skinner merely discloses treating apnea in neonates and does not disclose or suggest treating, preventing, or managing apnea or apnea disorders using norcisapride or a stereoisomer thereof. At most the disclosure of McCullough in combination with Skinner may merely render it "obvious to try" (+) norcisapride to treat, prevent, or manage apnea or apnea disorders. However, as the Examiner is aware, however, "obvious to try" is not the proper test for obviousness. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986). Rather, the proper test for obviousness is whether one skilled in the art would have a reasonable expectation of successfully completing the claimed invention. *See In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). As set forth above, the cited references do not provide one of ordinary skill in the art with the legally required reasonable expectation of success in arriving at the methods of the pending claims.

### **Conclusion**

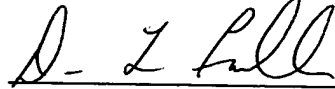
The combination of references cited by the Examiner does not suggest a method of treating, preventing, or managing apnea or apnea disorders using (+) norcisapride. Moreover, the references fail to provide the required reasonable suggestion or expectation of successfully arriving at the claimed invention.

For any of the reasons stated above, it is respectfully submitted that the rejection of claims 55-64 and 71 under 35U.S.C. § 103 should be withdrawn.

No fee is believed due for this submission. However, should any fee be due, please charge such fee to Pennie & Edmonds LLP Deposit Account No.16-1150.

Respectfully submitted,

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Enclosure